

We claim:

1. An apparatus for controlling a stream of liquid packages, each liquid package comprising a plurality of liquid and air segments, the apparatus comprising:

a probe for selectively aspirating liquid segments and air segments into a first  
5 fluid conduit in a plurality of cycles, each cycle ending with the aspiration of a final liquid segment and a final air segment in that order;

a second fluid conduit;

a valve coupled to said first fluid conduit and said second fluid conduit, said valve  
being adapted to be actuated between a first position in which said second fluid conduit is  
coupled to said first fluid conduit and a second position in which said second fluid conduit is not  
coupled to said first fluid conduit;

an air and liquid interface detector positioned along said second fluid conduit a  
fixed distance from said valve, said fixed distance corresponding to a predetermined fixed  
volume within said second fluid conduit; and

means for stopping the aspiration of the final air segment in a current cycle when  
said air and liquid interface detector detects an interface between an air segment and a liquid  
segment of a previous cycle which have moved into said second fluid conduit after the final  
liquid segment of said previous cycle has fully entered said second fluid conduit and for  
actuating said valve from said first position to said second position at a time subsequent to said  
20 detection.

2. An apparatus according to claim 1, wherein said liquid segment of a previous  
cycle which has moved into said second fluid conduit comprises the final liquid segment of said  
previous cycle and wherein said air segment of a previous cycle which has moved into said

second fluid conduit comprises an intermediate air segment aspirated just prior to the final liquid segment of said previous cycle.

3. An apparatus according to claim 2, wherein said predetermined fixed volume is substantially equal to a sum of an accurately metered volume of said final liquid segment and an optimal volume of said final air segment.

4. An apparatus according to claim 1, wherein said liquid segment of a previous cycle which has moved into said second fluid conduit comprises the final liquid segment of said previous cycle and wherein said air segment of a previous cycle which has moved into said second fluid conduit comprises the final air segment of said previous cycle.

5. An apparatus according to claim 4, wherein said predetermined fixed volume is substantially equal to an optimal volume of said final air segment.

6. An apparatus according to claim 1, wherein said valve comprises a shear valve.

7. An apparatus according to claim 1, wherein said air and liquid interface detector comprises a bubble detector.

8. An apparatus according to claim 1, wherein each of said cycles begins with the aspiration of a first air segment, wherein the final air segment and the first air segment in successive cycles have an optimal combined volume, and wherein said means for stopping causes the final air segment of said current cycle to have a first volume, said apparatus further comprising means for controlling the aspiration of the first air segment of a next successive cycle after said current cycle such that the first air segment of said next successive cycle has a volume equal to said optimal combined volume minus said first volume.

9. An apparatus according to claim 1, further comprising an aspirating pump coupled to said second fluid conduit.

10. An apparatus according to claim 1, wherein said liquid segments and said air segments are able to move from said first fluid conduit to said second fluid conduit when said valve is in said first position.

11. An apparatus according to claim 1, wherein each of said cycles begins with the aspiration of a first air segment and a first liquid segment in that order, the apparatus further comprising:

a third fluid conduit into which the liquid and air segments aspirated in each of said cycles are inserted and in which the stream of liquid packages is repeatedly bi-directionally flowed in a forward and a reverse direction, said third fluid conduit being coupled to said valve such that when said valve is in said second position said third fluid conduit is coupled to said second fluid conduit;

a second air and liquid interface detector positioned along said third fluid conduit adjacent said valve; and

means for stopping said flow of said stream of liquid packages in said reverse direction at a point in time when said second air and liquid interface detector detects an interface between the first air segment and the first liquid segment most recently inserted into said third fluid conduit adjusted by a delay, said delay being normalized around a predetermined nominal center point delay according to a feedback loop.

12. An apparatus according to claim 11, wherein said valve comprises a shear valve.

13. An apparatus according to claim 11, wherein said air and liquid interface detector comprises a bubble detector.

14. An apparatus according to claim 11, said feedback loop being based upon a time differential TD equal to  $T_2 - T_1$ , wherein  $T_1$  is a time at which a first particular liquid segment of a particular liquid package reaches a reference during said flow of said stream in said forward direction and  $T_2$  is a time at which a second particular liquid segment of said particular liquid package reaches said reference during said flow of said stream in said reverse direction.

15. An apparatus according to claim 14, said delay being calculated according to the following formula:

$$\text{Delay} = \text{CP} - \text{Error} * K,$$

wherein CP is said predetermined nominal center point delay, Error is equal to a predetermined set point minus TD, and K is a gain factor.

16. An apparatus according to claim 14, wherein said reference point comprises a third air and liquid interface detector positioned along said third fluid conduit.

17. An apparatus according to claim 11, wherein the liquid and air segments aspirated in each of said cycles and inserted into said third fluid conduit each comprise a liquid package having a length, wherein said length is measured for a plurality of said liquid packages during said flow of said stream in either said forward or said reverse direction and wherein an average length is calculated using a plurality of said measured lengths, said feedback loop being based upon a difference between a target liquid package length and said average length.

18. An apparatus according to claim 17, said delay being calculated according to the following formula:

$$\text{Delay} = \text{CP} - \text{Error} * K,$$

wherein CP is said predetermined nominal center point delay, Error is equal to said target liquid  
5 package length minus said average length, and K is a gain factor.

19. An apparatus for controlling a stream of liquid packages, each liquid package comprising a plurality of liquid and air segments, the liquid packages being formed in one or more cycles of aspiration of liquid and air segments, each cycle beginning with the aspiration of a first air segment and a first liquid segment, the apparatus comprising:

a fluid conduit into which the liquid and air segments aspirated in each of said cycles are inserted and in which the stream of liquid packages is repeatedly bi-directionally flowed in a forward and a reverse direction;

a valve coupled to a first end of said fluid conduit;

an air and liquid interface detector positioned along said fluid conduit adjacent  
15 said valve; and

means for stopping said flow of said stream of liquid packages in said reverse direction at a point in time when said air and liquid interface detector detects an interface between the first air segment and the first liquid segment most recently inserted into said fluid conduit adjusted by a delay, said delay being normalized around a predetermined nominal center  
20 point delay according to a feedback loop.

20. An apparatus according to claim 19, wherein said valve comprises a shear valve.

21. An apparatus according to claim 19, wherein said air and liquid interface detector comprises a bubble detector.

22. An apparatus according to claim 19, said feedback loop being based upon a time difference TD equal to  $T_2 - T_1$ , wherein  $T_1$  is a time at which a first particular liquid segment of a particular liquid package reaches a reference point during said flow of said stream in said forward direction and  $T_2$  is a time at which a second particular liquid segment of said particular liquid package reaches said reference point during said flow of said stream in said reverse direction.

23. An apparatus according to claim 22, said delay being calculated according to the following formula:

$$\text{Delay} = \text{CP} - \text{Error} * K,$$

wherein CP is said predetermined nominal center point delay, Error is equal to a predetermined set point minus TD, and K is a gain factor.

24. An apparatus according to claim 22, wherein said reference point comprises a second air and liquid interface detector positioned along said fluid conduit.

25. An apparatus according to claim 24, wherein said liquid packages are suitable for conducting an immunoassay analysis, wherein said first particular liquid segment comprises a third reagent into which a plurality of magnetic particles have been transferred, wherein said second particular segment comprises a second wash, wherein said second air and liquid interface detector is positioned adjacent a luminometer, said luminometer being positioned along said fluid conduit, and wherein said particular liquid package is a liquid package located within said fluid conduit closest to said air and liquid interface detector and said luminometer.

26. An apparatus according to claim 19, wherein the liquid and air segments aspirated in each of said cycles and inserted into said fluid conduit each comprise a liquid package having a length, wherein said length is measured for a plurality of said liquid packages during said flow of said stream in either said forward or said reverse direction and wherein an average length is calculated using a plurality of said measured lengths, said feedback loop being based upon a difference between a target liquid package length and said average length.

27. An apparatus according to claim 26, said delay being calculated according to the following formula:

$$\text{Delay} = \text{CP} - \text{Error} * K,$$

wherein CP is said predetermined nominal center point delay, Error is equal to said target liquid package length minus said average length, and K is a gain factor.

28. A method for controlling a stream of liquid packages, each liquid package comprising a plurality of liquid and air segments, the method comprising:

selectively aspirating liquid segments and air segments into a first fluid conduit in a plurality of cycles, each cycle ending with the aspiration of a final liquid segment and a final air segment in that order, said first fluid conduit being coupled to a valve, said valve being coupled to a second fluid conduit, wherein said valve is adapted to be actuated between a first position in which said first fluid conduit is coupled to said second fluid conduit and a second position in which said first fluid conduit is not coupled to said second fluid conduit;

detecting an interface between an air segment and a liquid segment of a previous cycle which have moved into said second fluid conduit at a position along said second fluid conduit which is a fixed distance from said valve after the final liquid segment of said previous

cycle has fully entered said second fluid conduit, said fixed distance corresponding to a predetermined fixed volume within said second fluid conduit; and

stopping the aspiration of the final air segment in a current cycle when said interface has been detected and actuating said valve from said first position to said second position at a time subsequent to said detection.

29. A method according to claim 28, wherein said detecting step is performed by an air and liquid interface detector.

30. A method according to claim 28, wherein said valve comprises a shear valve.

31. A method according to claim 28, wherein said liquid segment of a previous cycle which has moved into said second fluid conduit comprises the final liquid segment of said previous cycle and wherein said air segment of a previous cycle which has moved into said second fluid conduit comprises an intermediate air segment aspirated just prior to the final liquid segment of said previous cycle.

32. A method according to claim 31, wherein said predetermined fixed volume is substantially equal to a sum of an accurately metered volume of said final liquid segment and an optimal volume of said final air segment.

33. A method according to claim 28, wherein said liquid segment of a previous cycle which has moved into said second fluid conduit comprises the final liquid segment of said previous cycle and wherein said air segment of a previous cycle which has moved into said second fluid conduit comprises the final air segment of said previous cycle.



34. A method according to claim 33, wherein said predetermined fixed volume is substantially equal to an optimal volume of said final air segment.

35. A method according to claim 28, wherein each of said cycles begins with the aspiration of a first air segment, wherein the final air segment and the first air segment in successive cycles have an optimal combined volume, and wherein said stopping step causes the final air segment to have a first volume, said method further comprising controlling the aspiration of the first air segment of a next successive cycle after said current cycle such that the first air segment of said next successive cycle has a volume equal to said optimal combined volume minus said first volume.

36. A method according to claim 28, wherein each of said cycles begins with the aspiration of a first air segment and a first liquid segment in that order, the method further comprising:

inserting the liquid segments and the air segments aspirated in each of said cycles into a third fluid conduit such that for each of said cycles the first liquid segment and the first air segment are the next-to-last and the last liquid and air segment, respectively, inserted;

flowing said stream of liquid packages in a forward direction and a reverse direction in said third fluid conduit, said third fluid conduit being coupled to said valve such that when said valve is in said second position said third fluid conduit is coupled to said second fluid conduit;

detecting an interface between the first air segment and the first liquid segment most recently inserted into said third fluid conduit at a reference location along said third fluid conduit adjacent said valve when said stream is flowing in said reverse direction; and

stopping said flow of said stream at a point in time when said interface is detected  
adjusted by a delay, said delay being normalized around a predetermined nominal center point  
delay according to a feedback loop.

37. A method according to claim 36, further comprising actuating said valve after  
5 said flow of said stream is stopped.

38. A method according to claim 36, wherein said valve comprises a shear valve.

39. A method according to claim 36, said feedback loop being based upon a time  
difference TD equal to  $T_2 - T_1$ , wherein  $T_1$  is a time at which a first particular liquid segment of a  
particular liquid package reaches a reference point during said flow of said stream in said  
forward direction and  $T_2$  is a time at which a second particular liquid segment of said particular  
liquid package reaches said reference point during said flow of said stream in said reverse  
direction.

40. A method according to claim 39, said delay being calculated according to the  
following formula:

$$\text{Delay} = \text{CP} - \text{Error} * K,$$

wherein CP is said predetermined nominal center point delay, Error is equal to a predetermined  
set point minus TD, and K is a gain factor.

41. A method according to claim 36, wherein said detecting step is performed using  
an air and liquid interface detector positioned at said reference location.

42. A method according to claim 36, wherein the liquid and air segments aspirated in  
each of said cycles and inserted into said third fluid conduit each comprise a liquid package

having a length, wherein said length is measured for a plurality of said liquid packages during said flow of said stream in either said forward or said reverse direction and wherein an average length is calculated using a plurality of said measured lengths, said feedback loop being based upon a difference between a target liquid package length and said average length.

5           43.    A method according to claim 42, said delay being calculated according to the following formula:

$$\text{Delay} = \text{CP} - \text{Error} * \text{K},$$

wherein CP is said predetermined nominal center point delay, Error is equal to said target liquid package length minus said average length, and K is a gain factor.

10           44.    A method for controlling a stream of liquid packages, each liquid package comprising a plurality of liquid and air segments, the method comprising:

selectively aspirating liquid segments and air segments in a plurality of cycles, each cycle beginning with a first air segment and a first liquid segment;

15               inserting the liquid segments and the air segments aspirated in each of said cycles into a fluid conduit having a first end such that for each of said cycles the first liquid segment and the first air segment are the next-to-last and the last liquid and air segment, respectively, inserted;

flowing said stream of liquid packages in a forward direction and a reverse direction in said fluid conduit;

20               detecting an interface between the first air segment and the first liquid segment most recently inserted into said fluid conduit at a reference location along said fluid conduit adjacent said first end of said fluid conduit when said stream is flowing in said reverse direction; and

stopping said flow of said stream at a point in time when said interface is detected  
adjusted by a delay, said delay being normalized around a predetermined nominal center point  
delay according to a feedback loop.

45. A method according to claim 44, wherein said first end of said fluid conduit is  
5 coupled to a valve, the method further comprising actuating said valve after said flow of said  
stream is stopped.

46. A method according to claim 45, wherein said valve comprises a shear valve.

47. A method according to claim 44, said feedback loop being based upon a time  
difference TD equal to  $T_2 - T_1$ , wherein  $T_1$  is a time at which a first particular liquid segment of a  
10 particular liquid package reaches a reference point during said flow of said stream in said  
forward direction and  $T_2$  is a time at which a second particular liquid segment of said particular  
liquid package reaches said reference point during said flow of said stream in said reverse  
direction.

48. A method according to claim 47, said delay being calculated according to the  
15 following formula:

$$\text{Delay} = \text{CP} - \text{Error} * K,$$

wherein CP is said predetermined nominal center point delay, Error is equal to a predetermined  
set point minus TD, and K is a gain factor.

49. A method according to claim 44, wherein said detecting step is performed using  
20 an air and liquid interface detector positioned at said reference location.

50. A method according to claim 44, wherein the liquid and air segments aspirated in each of said cycles and inserted into said fluid conduit each comprise a liquid package having a length, wherein said length is measured for a plurality of said liquid packages during said flow of said stream in either said forward or said reverse direction and wherein an average length is calculated using a plurality of said measured lengths, said feedback loop being based upon a difference between a target liquid package length and said average length.

51. A method according to claim 50, said delay being calculated according to the following formula:

$$\text{Delay} = \text{CP} - \text{Error} * K,$$

wherein CP is said predetermined nominal center point delay, Error is equal to said target liquid package length minus said average length, and K is a gain factor.

52. A method for controlling a stream of liquid and air segments, comprising:  
selectively aspirating liquid segments and air segments into a first fluid conduit in a plurality of cycles, each cycle beginning with the aspiration of a first air segment and ending with the aspiration of a final air segment, said first and final air segments each having a volume;  
transferring the liquid segments and the air segments of each cycle from said first fluid conduit to a second fluid conduit;  
adjusting the volume of the final air segment of each cycle after the final air segment has moved into said second fluid conduit;  
transferring the liquid segments and the air segments of each cycle from said second fluid conduit to a third fluid conduit; and  
adjusting the volume of the first air segment of each cycle after the first air segment has moved into said third fluid conduit.

53. A method according to claim 52, wherein the volume of the final air segment of each cycle is adjusted to equal an optimal volume for the final air segment.

54. A method according to claim 52, wherein the volume of the first air segment of each cycle is adjusted according to a feedback loop.

5 55. An apparatus for controlling a stream of liquid and air segments, comprising:  
means for aspirating liquid segments and air segments into a first fluid conduit in  
a plurality of cycles, each cycle beginning with the aspiration of a first air segment and ending  
with the aspiration of a final air segment, said first and final air segments each having a volume;  
a second fluid conduit, said second fluid conduit being selectively coupled to said  
10 first fluid conduit such that said liquid segments and said air segments of each cycle move from  
said first fluid conduit to said second fluid conduit;  
means for adjusting the volume of the final air segment of each cycle after the  
final air segment has moved into said second fluid conduit;  
a third fluid conduit, said third fluid conduit being selectively coupled to said  
15 second fluid conduit such that said liquid segments and said air segments of each cycle move  
from said second fluid conduit to said third fluid conduit; and  
means for adjusting the volume of the first air segment of each cycle after the first  
air segment has moved into said third fluid conduit.

20 56. An apparatus according to claim 55, wherein the volume of the final air segment  
of each cycle is adjusted to equal an optimal volume for the final air segment.

57. An apparatus according to claim 55, wherein the volume of the first air segment  
of each cycle is adjusted according to a feedback loop.